Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

MFOLFOX6+PEMB Regimen

Folinic Acid (Leucovorin)-Fluorouracil-Oxaliplatin-Pembrolizumab

Disease Site

Gastrointestinal
Gastric / Stomach

Intent

Palliative

Regimen Category

Evidence-informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

This **Regimen Abstract** is an **abbreviated** version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Rationale and Uses

First-line treatment in patients with locally advanced unresectable or metastatic HER2-negative gastric adenocarcinoma

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B - Drug Regimen

Pembrolizumab every 6 weeks:

pembrolizumab[1,2]	400 mg	IV	Day 1; Every 6 weeks

(This drug is not currently publicly funded for this regimen and intent)

And mFOLFOX6 every 2 weeks:

oxaliplatin	85 mg /m²	IV	Day 1
leucovorin	400 mg /m²	IV (concurrently with oxaliplatin)	Day 1
fluorouracil	400 mg /m²	IV bolus, after leucovorin	Day 1

Then,

fluorouracil	2400 mg /m²	IV continuous infusion over 46 hours (single dose)	Start on Day 1

[1]Alternative pembrolizumab dosing schedule is 200 mg IV q 3 weeks.

[2]Give pembrolizumab before chemotherapy when given on the same day.

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C - Cycle Frequency

MFOLFOX6: Repeat every 2 weeks
Until disease progression or unacceptable toxicity^
(In the KEYNOTE-859 clinical trial, oxaliplatin (in XELOX+PEMB) may be discontinued after 6 cycles according to local guidelines.)

PEMBROLIZUMAB: Repeat every 6 weeks (400 mg dose)†
Until disease progression or unacceptable toxicity, or up to a maximum of 2 years, whichever occurs first

^If chemotherapy is discontinued after at least 1 cycle due to intolerance, pembrolizumab may be continued as single agent (PEMB(MNT)) for up to 2 years, unless disease progression or unacceptable toxicity.

†Alternative pembrolizumab dosing schedule is 200mg IV every 3 weeks.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Pembrolizumab Premedication (prophylaxis for infusion reactions):

- Routine pre-medication is not recommended.
- May consider antipyretic and H1-receptor antagonist in patients who experienced a grade 1-2 infusion reaction.

Oxaliplatin Premedication (prophylaxis for infusion reactions):

- There is insufficient evidence that routine prophylaxis with pre-medications reduces IR rates.
- Consider corticosteroids and H1-receptor antagonists ± H2-receptor antagonists in high-risk patients (i.e. ≥ cycle 6, younger age, female gender, prior platinum exposure, platinum-free interval ≥ 3 years).

Other Supportive Care:

- Also refer to CCO Antiemetic Recommendations.
- Avoid the use of corticosteroids or immunosuppressants before starting pembrolizumab

treatment.
- Avoid mucositis prophylaxis with ice chips as cold temperatures can precipitate or exacerbate acute neurological symptoms of oxaliplatin.

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J - Administrative Information

Approximate Patient Visit	3 to 4 hours
Pharmacy Workload (average time per visit)	49.356 minutes
Nursing Workload (average time per visit)	79.167 minutes

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K - References

Fluorouracil drug monograph. Ontario Health (Cancer Care Ontario).

Oxaliplatin drug monograph. Ontario Health (Cancer Care Ontario).

Pembrolizumab drug monograph. Ontario Health (Cancer Care Ontario).

Rha SY, Oh DY, Yañez P, et al. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for HER2-negative advanced gastric cancer (KEYNOTE-859): a multicentre, randomised, double-blind, phase 3 trial. Lancet Oncol 2023 Nov;24(11):1181-95. doi: 10.1016/S1470-2045(23)00515-6.

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L - Other Notes

DPD Deficiency Testing and Guidance

Patients should be tested for DPD deficiency before starting treatment with fluorouracil. Refer to the DPD Deficiency Guidance for Clinicians for more information.

In patients with unrecognized DPD deficiency, acute, life-threatening toxicity may occur; if acute grade 2-4 toxicity develops, treatment should be stopped immediately and permanent discontinuation considered based on clinical assessment of the toxicities.

Antidote for Fluorouracil Overdose:

Uridine triacetate is a prodrug of uridine and is a specific antidote for treating fluorouracil overdose or severe early onset toxicities. If available, consider administering as soon as possible (i.e. within 96 hours) for suspected overdose. If not available, treatment is symptomatic and supportive.

For usage approval and supply, contact Health Canada's Special Access Program (SAP) (Phone: 613-941-2108. On-call service is available for emergencies). Uridine triacetate (Vistogard®) is supplied by its manufacturer in the United States.

The recommended dosing and administration for **uridine triacetate** in patients ≥18 years is:

- 10 grams (1 packet of coated granules) orally every 6 hours for 20 doses in total, without regards to meals.
- Granules should not be chewed. They should be mixed with 3 to 4 ounces of soft foods such as applesauce, pudding or yogurt.
- The dose should be ingested within 30 minutes of preparation, followed by at least 4 ounces of water.
- Refer to the prescribing information on dose preparation for NG-tube or G-tube use.

Additional resources on the management of fluorouracil infusion overdose:

- Management of Fluorouracil Infusion Overdose Guideline (Alberta Health Services)
- Management of Fluorouracil Infusion Overdose at the BCCA - Interim Guidance (BC Cancer Agency)

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

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Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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